Citation:

Tay J, Brinkworth GD, Noakes M, Keogh J, Clifton PM. Metabolic effects of weight loss on a very-low-carbohydrate diet compared with an isocaloric high-carbohydrate diet in abdominally obese subjects.*J Am Coll Cardiol.* 2008;51(1):59-67.

PubMed ID: 18174038

Study Design:

Randomized Clinical Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare, under isocaloric and well-controlled diet conditions, weight loss and the metabolic effects at 6 months of a moderate energy-restricted very-low-carbohydrate, high-fat (VLCHF) diet and a high-carbohydrate, low-fat (HCLF) diet in abdominally obese subjects with elevated cardiovascular risk.

Inclusion Criteria:

- Men and women aged 18 to 65 years
- With abdominal obesity and the presence of at least 1 additional metabolic syndrome risk factor
- Written informed consent

Exclusion Criteria:

- History of liver, cardiovascular, peripheral vascular, respiratory, or gastrointestinal disease; diabetes or a malignancy

Description of Study Protocol:

Recruitment

Abdominally obese subjects were recruited by public advertisement.

Design: Randomized clinical trial

Blinding used (if applicable): not described

Intervention (if applicable)

- Subjects were matched for age, gender, and BMI and randomly assigned to either a VLCHF or HCLF diet for 24 weeks
- VLCHF diet: 4% of total energy as carbohydrate, 35% as protein, 61% as total fat (20% saturated fat); carbohydrate intake was restricted to<20 g/d during the first 8 weeks of the study and subjects were then given the option to increase carbohydrate intake to<40 g/d for the remaining 16 weeks.
- HCLF diet: 46% of total energy as carbohydrate, 24% as protein, 30% as total fat (<8% saturated fat); subjects were asked to restrict saturated fat intake to<10 g/day for the study duration.
- The diets were designed to be isocaloric, with a moderate energy restriction of ≈30% (≈6,000 kJ for women, ≈7,000 kJ for men).
- Key food items were supplied fortnightly for the first 8 weeks. These foods were uncooked but preweighed to provide about 30% of total energy. In the subsequent 16 weeks, $40 food vouchers were provided to subjects monthly.
- Subjects attended the clinic fortnightly for 8 weeks, monthly thereafter for dietetic consultations and a weight check to quantify time-course changes.
- No specific recommendations were given for physical activity.

Statistical Analysis

- Independent *t* tests for continuous variables and Pearson chi-square test for categorical variables were used to compare differences in baseline characteristics between groups.
- ANOVA was used to assess the effects of dietary intervention by comparing changes on the dependant variables between the groups over time.
- Where there was a significant main effect, post-hoc comparisons were performed with Bonferroni's adjustment for multiple comparisons to determine differences between group means.
- Intention-to-treat (ITT) analysis was performed to examine the change in weight from baseline to week 24.
- Pearson correlation analyses were conducted to assess the association of change between variables.
- Statistical significance was set at P≤0.05.

Data Collection Summary:

Timing of Measurements

- At weeks 0 and 24, after an overnight fast, body weight, height (baseline only), and blood pressure were measured before a venous blood sample for the determination of fasting glucose, insulin, lipids, apolipoprotein B (apoB), C-reactive protein (CRP) and plasma ketones.
- At weeks 0 and 24, dietary intake was assessed using a food frequency questionnaire. During the study, diet composition was assessed using 3-day food records recorded every 2 weeks.
- Physical activity was assessed using an established questionnaire.

Dependent Variables

- Weight loss
- Blood pressure
- Serum lipids, apoB and CRP

- Fasting glucose and insulin

Independent Variables

- Very-low-carbohydrate, high-fat diet
- High-carbohydrate, low-fat diet

Control Variables

- Energy intake
- Dietary adherence
- Gender
- Physical activity

Description of Actual Data Sample:

Initial N: 122 men and women

Attrition (final N): 88, indicating 28% dropout rate

Age: 18 to 65 years

Ethnicity: not described

Other relevant demographics:

Subjects who withdrew before the end of the study were similar to those who completed the study for age, gender distribution, BMI, waist circumference, and other CVD risk factors at baseline (P≥0.22).

Anthropometrics: Baseline characteristics (e. g., BMI, weight and waist circumference) were not significantly different between diet groups.

Location: Australia

Summary of Results:

Key Findings

- 88 subjects were included in data analysis indicating 28% dropout rate.
- High dietary compliance evidenced by dietary data and plasma ketones response
- Weight loss was similar in both diet groups (VLCHF -11.9±6.3 kg, HCLF -10.1±5.7 kg; P=0.17).
- Blood pressure, CRP, fasting glucose, and insulin reduced similarly with weight loss in both diets.
- The VLCHF diet produced greater decreases in triacylglycerols (VLCHF -0.64±0.62 mmol/l, HCLF -0.35±0.49 mmol/l; P=0.01) and increases in HDL-C (VLCHF 0.25±0.28 mmol/l, HCLF 0.08±0.17 mmol/l; P=0.002).
- LDL-C decreased in the HCLF diet but remained unchanged in the VLCHF diet (VLCHF 0.06±0.58 mmol/l, HCLF -0.46±0.71 mmol/l; P<0.001).
- A high degree of individual variability for the LDL response in the VLCHF diet was observed, with 24% of individuals reporting an increase of at least 10%.
- The apoB levels remained unchanged in both diet groups.

Author Conclusion:

After 6 months, isocaloric energy-restricted VLCHF and HCLF diets result in similar weight loss. Although both diets had similar improvements for a number of metabolic risk markers, an HCLF diet had more favorable effects on the blood lipid profile. This suggests that the potential long-term effects of the VLCHF diet for CVD risk remain a concern and that blood lipid levels should be monitored.

Reviewer Comments:

28% dropout rate, but subjects who withdrew before the end of the study were similar to those who completed the study in terms of age, gender, BMI, waist circumference, and other CVD risk factors at baseline. Abdominal obesity was not well defined in inclusion criteria.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes

2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No

5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes

8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes